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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/578,453	05/26/2000	Jacques Mallet	03804.0114-02	9203

5487 7590 04/11/2002

AVENTIS PHARMACEUTICALS, INC.
PATENTS DEPARTMENT
ROUTE 202-206, P.O. BOX 6800
BRIDGEWATER, NJ 08807-0800

EXAMINER
SHUKLA, RAM R

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 04/11/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

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Commissioner of Patents and Trademarks

DETAILED ACTION

During a telephonic conversation, Applicants' representative Mr. Todd Rams indicated that the references cited in the 103 rejection of claims 16, 17, 19, 20, 21, 22, 25, and 26 were not the same as those cited in the form paragraph of the rejection and that there references were not provided with the action. Mr. Rams requested a new office action with corrections made. Accordingly, the office action of 1-2-02 is withdrawn and a new office action is being issued.

The Examiner prosecuting this application has been changed. Any inquiries relating to the examination of the application should be directed to Examiner Shukla, whereas any inquiries relating to formal matters should be directed to Ms. Pinkney, Patent Analyst. The phone numbers for Examiner Shukla and Patent Analyst Pinkney are provided at the end of this office action.

1. Applicant's election with traverse of the invention of group I, claims 16-22, 25, and 26 pertaining to a recombinant virus comprising a nucleic acid encoding a mutated form of p53 and its use in vitro in Paper No. 10 is acknowledged. The traversal is on the ground(s) that the restriction of invention in a claim violates the applicants right to claim their invention as they choose and in support they have cited In re Weber. Furthermore, the applicants have argued that the office provided no reasons or examples as required by MPEP 803 to support its conclusion that the recombinant viruses recited by the claims in groups I, II, and III are different inventions and that no basis for concluding that the search presented undue burden was provided. This is not found persuasive because the applicants have only partially quoted the case law. It is noted that In re Weber court stated that 35 USC 121 gives the office authority to restrict an application to one of several claimed inventions that are found to be independent and distinct and such is the case in the instant application. It is noted that the office did not reject the claim therefore it is not clear as to what is the basis for applying the cited case law in the instant situation. Next, it is noted that the vector comprising a nucleic acid

that encodes a p53 mutant would have distinct utilities compared with a vector comprising a nucleic acid that has a site for binding of p53 to DNA or a nucleic acid that encodes an antisense RNA. For example, while an artisan can make a mutant p53 with the vector of group I, not such protein can be produced from the vectors of groups II or III. Additionally, the sequence structure of the nucleic acid of group I would be distinct from that of the nucleic acids of groups II or III. In other words, a search for the invention of group I would not be coextensive with that of groups II or III. Furthermore, the method of group IV does not use the vectors of any of the groups I-III, therefore, the search for the invention of group IV would not be coextensive with the search of any of the groups I-III. Finally, with regard to the issue of same classification, it is noted that all the genetically modified micro-organisms, cells, or viruses are classified in the cited class/subclass, however, this does not mean that all the microorganisms, cells and viruses are the same invention.

Therefore, the requirement is still deemed proper and is therefore made FINAL.

2. Claims 23, 24, and 27-31 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 10. It is noted that claims 16-22, 25, and 26 would be examined to the extent they encompass the elected invention of group I.

Regarding claim 18 it is noted that this claim does not recite the elected invention and therefore the claim is withdrawn from further considerations.

3. Claims 16, 17, 19-22, and 25-26 are under consideration.

Claim Objections

4. Claims 16-22, 25, and 26 are objected to because they recite a non-elected invention. Applicants are required to amend the claims to reflect the invention elected for prosecution.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 19 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is noted that the claim 19 recites a recombinant virus of claim 16 that comprises two nucleic acids selected from a list of three different nucleic acids, however, after withdrawing the invention pertaining to groups II and III, there is only one nucleic acid left and therefore it is not clear what is the second nucleic acid in the vector.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 16, 17, 19, 20, 21, 22, 25, and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Michalovitz et al (Cell 62: 671-680, 1990) in view of Moberg et al (Journal of Cellular Biochemistry 49:208-215, 1992) and La Gal La Salle (Science 259: 988-990, 1993).

The claimed invention is drawn a recombinant virus comprising a nucleic acid encoding a mutant P53 protein, wherein the virus is selected from the group of an adenovirus, a herpes virus, and a adeno-associated virus, the nucleic acid is p53Val135 mutant, a method of inhibiting toxicity in cultured neuronal cells and wherein the vector nucleic acid is in a vector and the vector is a replication defective virus.

At the time of the invention, Michalovitz et al taught the transfection of rat embryo fibroblasts with an expression vector encoding the p53Val135 mutant and that the mutant is a temperature sensitive mutant whose expression can be modulated by changing the temperature of the culture medium cells are grown (see the abstract, figure 1, table 1 and rest of the article). They further taught that this mutant suppresses oncogene-mediated transformation of the cells at 32.5 celcius, which showed that this mutant could function as wild type p53 (see the last paragraph in the left column on page 673 continued in the right) column. On the other hand this mutant functions as a mutant p53 in transforming cells in the presence of oncogenes at high temperature (the discussion on page 677). This art also teaches that a ts mutant of p53 would provide major clues toward understanding the mode of action of the protein (see last paragraph in left column on page 672). Micahlovitz et al does not teach a viral vector that comprises mutant p53.

Moberg et al taught that p53 repressed transcription of murine c-myc promoter in a human glian cell and that the mutant p53 did not suppress transcription of c-myc promoter (see the abstract). This art also teaches co-transfection of c-myc promoter construct with expression vectors expressing wild type or mutant p53 (see right column on page 211).

La Gal La Salle et al taught a replication defective adenoviral vector for gene transfer into neurons and into glia in the brain. They further taught that adenoviral vectors could be used for transferring gene in brain both in vitro and in vivo (see the first paragraph in left column on page 988) and that adenoviral vectors have several advantages for gene transfer, such as they can accommodate large inserts, have a larger host range, and low pathogenicity in humans and high titers could be produced.

It would have been obvious to an artisan of ordinary skill to make an adenoviral vector comprising a nucleic acid encoding a mutant p53, p53Val135, by modifying cloning the nucleic acid sequence of Michalovitz et al in the vector of La Gal La Salle et al and expressed the vector in a glial cell or neuronal cell with a reasonable expectation of success. An artisan of skill would have been motivated to

make such an adenoviral vector because the results of Michalovitz et al that p53Val135 behaved both as a wild type and a mutant p53 protein under different conditions and the results of Moberg et al that mutant p53 did not suppress c-myc promoter indicated different effects of mutant p53 and an artisan of skill would have been able to test the activity of the both wild type as well as mutant p53 using the same construct. An artisan would have been motivated to use adenoviral vector because La Gal La Salle et al teach that it has advantages over other vector for both in vitro or in vivo use. Regarding claims 25 and 26, it is noted that it would have been obvious to use the adenoviral vector comprising p53Val135 in identifying compounds that modify transformation induced by c-myc in ht glial or neuronal cells because of the temperature sensitive phenotype of the p53Val135 mutant.

9. No claim is allowed.

When amending claims, applicants are advised to submit a clean version of each amended claim (without underlining and bracketing) according to § 1.121(c). For instructions, Applicants are referred to http://www.uspto.gov/web/offices/dcom/olia/aipa/index.htm.

Applicants are also requested to submit a copy of all the pending/under consideration claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (703) 305-1677. The examiner can normally be reached on Monday through Friday from 7:30 am to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The fax phone number for this Group is (703) 308-4242. Any inquiry of a general nature, formal matters or relating to the status of this application or proceeding should be directed to the Dianiece Jacobs whose telephone number is (703) 305-3388.

Ram R. Shukla

RAM R. SHUKLA, PH.D
PATENT EXAMINER

Ram R. Shukla, Ph.D.